Remarks

Claims 1-13 and 21-27 were pending in the subject application. By this Amendment, claims 1, 3, 5-10, 12, 21, 26, and 27 have been amended, and new claims 28-30 have been added. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. Claims 4-6 and 12 remain pending but withdrawn from consideration. It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of the applicants' agreement with or acquiescence in the Examiner's position. Accordingly, claims 1-13 and 21-30 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

The applicants acknowledge that claims 4-6 and 12 have been withdrawn from further consideration as being drawn to a non-elected invention. However, the applicants wish to reserve the right to request rejoinder of the non-elected process claims upon an indication of an allowable compound claim in accordance with MPEP §821.04.

By this Amendment, claims 1, 3, 5-10, 12, 21, 26, and 27 have been amended, and new claims 28-30 have been added. Claims 28-30 read on the elected species.

The Office Action indicates that the disclosure of U.S. Provisional Application No. 60/319,780 fails to provide adequate support or enablement for one or more claims of the subject application. The applicants respectfully submit that the claimed invention is adequately described and enabled.

The Abstract has been objected to for containing the term "thereof". Submitted with this Amendment, on a separate page, is a substitute Abstract wherein the term "thereof" has been deleted. Entry and consideration of the Abstract in the subject application is respectfully requested. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 21-27 have been rejected under 35 U.S.C. §112, first paragraph, as containing new matter. The applicants respectfully traverse, and submit that claims 21-27 do not constitute new matter.

The applicants submit that the subject specification describes the invention of claims 21-27 in sufficient detail that one of ordinary skill in the art would reasonably conclude that the inventors had possession of the claimed invention. Support for claims 21-22 can be found, for example, at page 8, line 20; page 9, lines 18-20; page 25, lines 15-17 and 22-24; and page 27, lines 19-20, of the specification. Support for claims 23 and 24 can be found, for example, at page 2, lines 20-27; page 6, lines 18-21; page 7, lines 6-17; page 8, lines 20-24; and page 9, lines 14-20 of the subject specification. Support for new claims 25-27 can be found, for example, at page 25, lines 18-29 of the subject specification. The subject specification directs one of ordinary skill in the art to immediately envision the use of interfering RNA (RNAi) molecules, such as siRNA, specific for protein kinase C (PKC) mRNA.

As the Examiner is aware, rewording of a passage where the same meaning remains intact is not new matter. *In re Anderson*, 41 F.2d 1237; 176 USPQ 331 (CCPA 1973). The mere inclusion of an art recognized definition known at the time of filing an application is permissible. The applicants' specification need not describe the claimed invention in *ipsis verbis*. *Ex parte Sorenson*, 3USPQ2d, 1462, 1463 (Bd. Pat. App. & Inter., 1987). The test for determining whether a claimed invention is adequately described in the specification is whether the originally filed disclosure reasonably conveys to a person of ordinary skill in the art that the applicant had possession of the subject matter claimed. *Ipsis verbis* support is not required.

Based on the terms used in the specification to describe the genus of nucleic acid inhibitors of PKC expression (see, for example, pages 8, line 20; page 25, lines 15-17, and page 27, lines 19-20), including "siRNA", which are small interfering RNA, one of ordinary skill in the art reading the specification would immediately discern that an interfering RNA (RNAi) molecule could be used to interfere with translation of PKC mRNA, based on the teachings of the subject specification as a whole.

The applicants submit that the disclosure of the specification conveys with reasonable clarity to those skilled in the art that the inventors were in possession of the invention of claims 21-27. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 1-3, 7-11, 13, and 21-27 have been rejected under 35 U.S.C. §112, first paragraph, as lacking sufficient written description. The applicants traverse and respectfully submit that the subject specification provides a sufficient written description of the claimed invention.

As acknowledged in the Office Action, possession of a claimed genus can be established by providing, in the specification, sufficient distinguishing identifying characteristics of the genus. In addition to the two inhibitors referenced at page 5 of the Office Action (RO318220 and PKC-α/β pseudosubstrate peptide), the specification discloses many more PKC inhibitors, and classes of PKC inhibitors, which are representative of the claimed genus. The subject specification describes a multitude of PKC inhibitory molecules, such as those listed in claim 4, *i.e.*, AG 490, PD98059, staurosporine, Ro-31-7549, Ro-31-8425, Ro-32-0432, sangivamycin; calphostin C, safingol, D-erythro-sphingosine, chelerythrine chloride, melittin; dequalinium chloride, Go6976, Go6983, Go7874, polymyxin B sulfate; cardiotoxin, ellagic acid, HBDDE, 1-O-Hexadecyl-2-O-methyl-rac-glycerol, hypercin, K-252, NGIC-J, phloretin, piceatannol, tamoxifen citrate, flavopiridol, and bryostatin 1. The Examiner's attention is respectfully directed to page 7, lines 12-28; and page 8, lines 1-24, of the specification. For example, different classes of PKC inhibitors and their preparation, and/or commercial sources of availability are described in U.S. Patent Nos. 5,621,101; 5,621,098; 5,616,577; 5,578,590; 5,545,636; 5,491,242; 5,488,167; 5,481,003; 5,461,146; 5,270,310; 5,216,014; 5,204,370; 5,141,957; 4,990,519; and 4,937,232, which are incorporated by reference at page 41 of the specification. These patents teach PKC inhibitors such as quercetin (3,3',4',5,7-pentahydrdoxyflavone), tamoxifen, ilmofosin, and ET-18-OCH_3, staurosporine, bis-N-substituted derivatives of staurosporine, K-252a derivatives, sphingosines, sphinganines, lysosphingolipids, N-aminoalkyl amide compounds, furocoumarinsufonamide derivatives, substituted anthraquinones, and quinolyloxazole-2-ones. Many other inhibitors of PKC were also known in the art at the application's filing date. Various types of PKC inhibitors are described at page 8 of the specification, based on their mode of inhibition. Screening assays to identify other PKC inhibitors are described in the paragraph bridging pages 8-9 of the specification.

In addition to the chemical compounds listed above, various oligonucleotide inhibitors of PKC are known in the art. At page 10 of the application, U.S. Patent Application Publication 2003/0148989 (Bennet *et al.*), teaching oligonucleotide inhibition of PKC *in vivo* for treatment of

cancer and other diseases, is cited. The Examples in the Bennet *et al.* publication indicate that reduction of PKC expression and inhibition of tumor growth were achieved *in vivo*. Examples of U.S. patents describing oligonucleotide inhibitors of PKC and inhibition of PKC expression *in vivo* include, but are not limited to, Nos. 6,537,973; 6,339,066; 6,190,869; 6,117,847; 6,015,892; 5,959,096; 5,916,807; 5,885,970; 5,882,927; and 5,703,054. Furthermore, RNA interference-mediated inhibition of PKC-alpha expression, including target sequences within the human PKC-alpha gene and corresponding interfering nucleic acid sequences, are described in U.S. Patent Application Publication No. WO 03/070983 A1 (see, for example, Tables I and II at pages 116-121), for the treatment of cancer and other diseases. Submitted herewith for the Examiner's consideration as Exhibits A-C are mammalian orthology comparisons for the classical isoforms, PKC-alpha, PKC-beta, and PKC-gamma, respectively, obtained from the National Center for Biotechnology Information's (NCBI) Homologene database, which is a publicly available system for automated detection of homologs among the annotated genes of several completely sequenced eukaryotic genomes, and is utilized by those of ordinary skill in the art. Each Exhibit includes a table of pair wise alignment scores, showing levels of homology among humans and some other mammals. As shown in the Exhibits, each sequence has conserved regions and the degree of nucleotide homology between the human PKC and that of the other represented mammals is 89% or more. Having the structure and sequence of the target gene (PKC), the teachings of the specification, and many examples of nucleic acid inhibitors of PKC in the art, the applicants submit that one skilled in the art would readily envision target nucleic acid sequences with the recipient mammal's mRNA and corresponding inhibitory nucleic acid molecules.

At page 5, the Office Action indicates that the claims do not recite any specific structure of PKC inhibitor, such as a sequence of interfering RNA. As evidenced above, there is an abundance of chemical compounds and nucleic acid molecules known in the art which have established PKC inhibitory activity, several of which are specifically referred to in the specification. The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known and already available to the public. *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert.*

denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984).

Recognizing that the state of the art has sufficiently developed, the Federal Circuit has held that "the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it ... one of ordinary skill in the art at the time the ... application was filed may have therefore been in possession of the entire genus of DNA sequences that can encode the disclosed partial protein sequence, even if individual species within that genus might not have been described or rendered obvious". *In re Wallach*, 71 USPQ2d 1939; 378 F.3d 1330 (CAFC 2004). The Court also cited the Patent Office's Manual of Patent Examining Procedure (MPEP), which states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species. MPEP §2163.II.A.3.a.ii. (8th ed., rev. 2, 2001 and May, 2004).

"Moreover, we see no reason to require a patent applicant to list every possible permutation of the nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed, given the fact that it is, as explained above, a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that can encode it." *In re Wallach*, at 1942.

The nucleic acid PKC inhibitors recited in the claims are not described by function alone. Structural attributes of interfering RNA and antisense oligonucleotides, for example, including size and content, were known in the art at the time the application was filed. Furthermore, having the nucleotide sequence of the target gene provides discerning information regarding the sequences (*i.e.*, structural information) of other suitable inhibiting nucleic acid molecules, and leads one of ordinary skill in the art to their selection. Accordingly, the teaching of the subject specification, knowledge of

the sequence and structure of the PKC gene, and the nucleic acid PKC inhibitors that others have developed for treatment of other disease states provides sufficient structural and functional correlates to describe the genus of target PKC sequences and corresponding nucleic acid inhibitors. The Office Action appears to acknowledge that the state of the art at the subject application's filing date was sufficiently developed such that the design and use of RNAi molecules to inhibit expression of a target gene *in vitro* is well established (page 7, last paragraph, of the Office Action).

The written description requirement states that the applicant must describe the invention; it does not state that every invention must be described in the same way. The applicants acknowledge that sequences and structural formulas provide a convenient method of demonstrating possession of many molecules; however, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. An applicant may show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. MPEP§ 2163. In *Enzo Biochem, Inc. v. Gene-Probe, Inc.*, 63 USPQ2d 1609 (Fed Cir. 2002), the Court reaffirmed that deposit of a physical sample may replace words when description is beyond present scientific capability. In *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 65 USPQ2d 1385 (Fed Cir. 2003), the Court explained further that the written description requirement may be satisfied "if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." For example, possession of an antibody may be demonstrated based on a description and characterization of its corresponding antigen. Disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. *Noelle v. Lederman*, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) and MPEP 2163 IIA3(a).

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). There is no *per se* rule that an actual

reduction to practice must occur prior to filing, or that the need to screen for certain classes of candidate nucleic acid molecules precludes adequate written description of a broader genus of nucleic acid molecules. Possession may be shown in a variety of ways, including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, *e.g.*, MPEP §2163.02, *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). Compliance with the written description requirement is a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 963; 63 USPQ2d 1609, 1613 (Fed. Cir. 2002).

Due to their nature and the state of the art, the PKC inhibitors recited in the claims are clearly distinguishable from the chemical compounds at issue in *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (Fed. Cir. 2004), for example, in which the Court affirmed that the description of the cyclooxygenase-2 enzyme (COX-2) and an assay for identifying selective inhibitors of COX-2 did not provide an adequate written description of unknown non-steroidal molecules capable of selectively inhibiting the enzyme. A diversity of PKC inhibitors, including chemical compounds, and inhibitory nucleic acids, and their targets, were known in the art at the time the subject application was filed. The state of the art of PKC inhibitors provides one skilled in the art with a sufficient structural template and functional correlates to describe the genus of PKC inhibitors recited in the claims. The subject specification does not require the screening of vast amounts of candidate small molecules *de novo*, based on function alone, with no guidance provided or available as to the molecular structure of a receptor agonist to be identified. Rather, a diverse genus of PKC inhibitors was known and available at the application's filing date. Based on the teaching of the subject specification, the knowledge of the sequence and structure of the PKC gene and protein, and the knowledge of the various mechanisms utilized by known PKC inhibitors, together provide

sufficient structural and functional correlates to demonstrate possession of the PKC inhibitors recited in the claims. All functional descriptions of genetic or chemical material do not necessarily fail to meet the written description requirement as a matter of law. Rather, the Court has held that the written description requirement may be satisfied if, in the knowledge of the art, the disclosed function is sufficiently correlated to a particular, known structure. *Enzo Biochem, Inc.* Such is the case here. The written description requirement must be considered in the context of the claimed invention and the state of knowledge in the relevant art. *Capon et al. v. Eshhar et al.*, 418 F.3d, 1349 (Fed. Cir. 2005).

The fundamental concept of the invention is that PKC inhibition would be of benefit in inhibiting RSV infection, as taught in the subject application. The state of the art was sufficiently developed such that tools and methods for achieving the required PKC inhibition were appreciated by the inventors, taught in the patent application, and available to those of ordinary skill in the art. Thus, the applicants submit that the patent application contains sufficient disclosure to convey to one of ordinary skill in the art that the applicants had possession of the concept of what is claimed.

In view of the abundance of PKC inhibitors available at the time the subject application was filed, the application conveys with reasonable clarity to those skilled in the art that, as of the application's filing date, the applicants were in possession of the genera of PKC inhibitors suitable for inhibiting RSV infection, as recited in the claims. Thus, the applicants submit that the subject specification contains sufficient disclosure to convey to one of ordinary skill in the art that the applicants had possession of the claimed method. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 1-3, 7-11, 13, and 21-27 have been rejected under 35 U.S.C. §112, first paragraph, as non-enabled by the subject specification. The applicants respectfully traverse and submit that the claimed invention is fully enabled by the subject specification.

At page 9, the Office Action notes that the claims embrace any and all genera of siRNA molecules that decrease PKC. By this Amendment, claim 21 has been amended to clarify that the interfering RNA is targeted to PKC mRNA.

The Office Action indicates that the subject specification does not provide sufficient guidance to teach one skilled in the art to use the nucleic acid inhibitors such as interfering RNA

targeted to PKC mRNA *in vivo*. The applicants respectfully submit that the data in the Examples of the application establish the fundamental concept of the invention, *i.e.*, that PKC inhibition would be of benefit in inhibiting RSV infection. In particular, the data in the application shows that PKC activity is required for proper location of RhoA at the cell membrane for successful RSV infection. The state of the art was sufficiently developed such that tools and methods for achieving the required PKC inhibition were appreciated by the inventors, taught in the patent application, and available to those of ordinary skill in the art. Thus, the applicants submit that the patent application contains sufficient disclosure to enable one of ordinary skill in the art to carry out the methods of the invention without undue experimentation.

To the extent the applicants' remarks set forth above in response to the rejection under 35 U.S.C. §112, first paragraph, for lack of written description, are applicable to the non-enablement rejection, the remarks are incorporated herein by reference. A large variety of PKC inhibitors are described in the specification and/or were known in the art at the time the application was filed, such as chemical agents of various types (U.S. Patent Nos. 5,621,101; 5,621,098; 5,616,577; 5,578,590; 5,545,636; 5,491,242; 5,488,167; 5,481,003; 5,461,146; 5,270,310; 5,216,014; 5,204,370; 5,141,957; 4,990,519; and 4,937,232), antisense oligonucleotides (U.S. Patent Application Publication 2003/0148989; U.S. Patent Nos. 6,537,973; 6,339,066; 6,190,869; 6,117,847; 6,015,892; 5,959096; 5,916,807; 5,885,970; 5,882,927; and 5,703,054), and interfering RNA (U.S. Patent Application Publication No. WO 03/070983 A1). Also submitted herewith for the Examiner's consideration are Milhavet O. *et al.*, *Pharmacol. Rev.*, 2003, Dec., 55(4):629-648; Agrawal N. *et al.*, *Microbiol. Mol., Biol. Rev.*, 2003, Dec., 67(4):657-685); Kim V.N. *et al.*, *J. Korean Med. Sci.*, 2003, 18:309-318; Gitlin L. and Andino, *J. Virol.*, 2003, 77(13):7159-7165; Coburn G.A. and Cullen, *J. Antimicrobial Chemotherapy*, 2003, 51:753-756; Lieberman J. *et al.*, *Trends Mol. Med.*, 2003, 9(9):397-403; Reich S.J. *et al.*, *Molecular Vision*, 2003, 9:210-216; Scherr M. *et al.*, *Oligonucleotides*, 2003, 13:353-363; and Song E. *et al.*, *Nature Medicine*, 2003, 9(3):347-351, which describe gene silencing using interfering RNA *in vivo*.

As shown by the Milhavet *et al.*, and Agrawal *et al.*, and the other publications submitted herewith, many laboratories have had significant success in reducing endogenous and foreign gene expression in a large variety of cell types, using various RNA species and delivery methods (see, for

example, Table 1, at pages 635-636 of Milhavet *et al.*). Inhibition of viral replication has been achieved *in vitro* and *in vivo* using interfering RNA-mediated gene silencing, as demonstrated by Coburn G.A. and Cullen, *J. Virol.*, 2002, 76(18):9225-9231; Lee M-T M. *et al.*, *J. Virol.*, 2003, 77(22):11964-11972; Qing Ge *et al.*, *PNAS*, 100(5):2718-2723; McCaffrey A.P. *et al.*, *Nature*, 2002, 418(6893):38-39; McCaffrey A.P. *et al.*, *Nat. Biotechnol.*, 2003, 21(6):639-644; Hu W.Y. *et al.*, *Curr. Biol.*, 2002, 12(15):1301-1311; and Gitlin L. *et al.*, 2002, 418(6896):430-434, which are submitted herewith. Since the subject application was filed, RNAi-mediated gene silencing *in vivo* has been demonstrated in non-human primates (Zimmermann T.S. *et al.*, *Nature*, 2006, 441(7089):111-114; Tolentino M.J. *et al.*, *Retina*, 2004, 24:132-138, which are submitted herewith).

As the applicants stated above, having the structure and sequence of the target gene (PKC), the applicants submit that one skilled in the art could readily obtain target nucleic acid sequences with the recipient mammal's mRNA. Furthermore, due to the certainty of the genetic code and complementarity, there is a well known correlation between target nucleic acid sequences within a target gene and nucleic acid sequences that interfere with the expression of the target gene. Hence, having the nucleotide sequence of the target gene provides sufficient information to allow one skilled in the art to obtain candidate interfering RNA molecules without resort to undue experimentation. As shown by the Milhavet *et al.*, having the nucleotide sequence of the target gene provides discerning information regarding the sequences of suitable interfering RNA molecules, and leads one of ordinary skill in the art to their selection. As indicated by Milhavet *et al.*,

> All that is needed to implement siRNA-mediated silencing of expression of a gene of interest is the cDNA sequence of that gene, and commercially available reagents with which to perform the synthesis (Milhavet *et al.* page 637, column 1, lines 2-6).

The applicants respectfully submit that, in view of the disclosure of the subject specification as originally filed demonstrating that PKC inhibition would be of benefit in inhibiting RSV infection, and in view of the availability of a broad genus of PKC inhibitors, methods for reducing PKC expression using PKC inhibitors such as interfering RNA are fully enabled.

Inhibition of gene expression using nucleic acid inhibitors of various genes (including PKC) has been demonstrated in animal models of other disease states. All that is required by the patent laws is that a "reasonable correlation" exist between the scope of the claims and the scope of

enablement. *In re Brana*, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) and MPEP 2164.02. A rigorous or an invariable exact correlation is not required, as stated in *Cross v. Iizuka*, 224 USPQ 739, 747 (Fed. Cir. 1985):

> [B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.)

If a particular model is recognized as correlating to a specific condition, then it should be accepted as such unless there is evidence that the model does not correlate. Since the initial burden is on the Examiner to give reasons for lack of enablement, reasons must also be given for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. Thus, the applicants respectfully submit that the data within the specification is reasonably predictive of inhibition of RSV infection upon inhibition of PKC *in vivo*, and the animal models in the art are sufficiently predictive of PKC gene silencing *in vivo*. As such, the pending claims are commensurate in scope with the experimental findings of the instant disclosure and enabled thereby.

The applicants respectfully submit that an application for patent is not required to show that a claimed method of treatment of a disease condition results in a cure of that disease condition, or even that clinical efficacy is achieved. The Federal Circuit has made it clear that the showing for therapeutic utility that is sufficient to satisfy the patent laws is not to be confused or equated with the showing required by the Food & Drug Administration for drugs, medical devices, and procedures. *Scott v. Finney*, 32 USPQ2d 1115 (Fed. Cir. 1994) and Manual of Patent Examining Procedure 2164.05. Given the state of the art as demonstrated by the scientific publications submitted herewith, and the information provided in the subject specification and the experimental results obtained therewith, one of ordinary skill in the art can target and reduce expression of PKC *in vitro* or *in vivo*, without resort to undue experimentation. Thus, the applicants respectfully submit that the subject specification enables the methods as currently claimed.

Accordingly, the applicants respectfully submit that, given the teaching of the specification and the state of the art in gene suppression using agents such as interfering RNA, one of ordinary skill in the art could carry out the claimed methods using nucleic acid inhibitors of PKC such as

interfering RNA, or other PKC inhibitors, without the need for undue experimentation. In view of the foregoing remarks, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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GPL/mv
Attachments: Petition and Fee for Extension of Time
Replacement Abstract
Exhibits A-C
Milhavet *et al.*
Agrawal *et al.*
Kim V.N.
Gitlin L. and Andino
Coburn G.A. and Cullen (2003)
Lieberman J. *et al.*
Reich S.J. *et al.*
Scherr M. *et al.*
Song E. *et al.*
Coburn G.A. and Cullen (2002)
Lee M-T M. *et al.*
Qing Ge
McCaffrey A.P. *et al.*
McCaffrey A.P. *et al.*
Hu W.Y. *et al.*
Gitlin L. *et al.*
Zimmermann T.S.
Tolentino M.J. *et al.*